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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,205	02/20/1998	CARL H. JUNE	36119-126	2825

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/027,205	JUNE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/21/2008; 05/29/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *96,97 and 99-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *96, 97, 99-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Decision on Petition, mailed 05/29/2008, which granted the revival of the instant application pursuant to 37 CFR 1.137(b), is acknowledged.

2. Applicant's amendment, filed 03/21/2008, has been entered.

Claims 96-97 have been amended.

Claims 1-95 and 98 have been canceled previously.

Claims 96-97 and 99-107 are pending in the instant application.

3. Given applicant's statements concerning of common ownership at the time the invention was made,
the previous rejection under 35 U.S.C. § 103(a) based upon June et al. (U.S. Patent No. 6,352,694) ('694) (of record) AND/OR June et al. (U.S. Patent No. 6,905,680) ('680) has been withdrawn in view their lack of availability as prior art under 35 USC 103(c).

New Grounds of Rejection have been set forth herein.

The teachings of June et al. (U.S. Patent No. 6,352,694) OR June et al. (U.S. Patent No. 6,905,680) ('680) have been substituted with June et al. (WO 95/33823).

4. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 96-97 and 99-107 are rejected under 35 U.S.C. § 103(a) as being unpatentable over June et al. (WO 95/33823) in view of Chang et al. (U.S. Patent No. 6,129,916) (of record), Levine et al. (International Immunology 7: 891-904, 1995) (1449; #CI), Kwon et al. (U.S. Patent No. 5,569,997) (of record) and Allaway et al. (US 2004/0086528 A1) (of record).

June et al. teach and claim a method comprising activating a population of human T cell to proliferate by contacting the cells ex vivo and in vivo with an anti-human CD3 antibodies and anti-human CD28 antibodies (e.g., see pages 5-7and 10-15 and Examples 7-9), including immobilized antibodies (e.g., see page 11, paragraph 3 and Examples 7-9 on pages 34-35) as well as the applicability of such ex vivo and in vivo methods for patients with HIV (e.g., see page 2, paragraph 3; pages 21-24 on pages 34-35) (see entire document, including Summary of the Invention and Detailed Description of the Invention).

While June et al. clearly teaches the combination of anti-CD3 antibodies and anti-CD28 antibodies for stimulating T cells as well as applicability of immobilized antibodies,
Chang et al. and Levine et al. provide a more explicit teaching of beads comprising multiple antibody specificities, including anti-CD3 antibodies and anti-CD28 antibodies.

As previously noted, Chang teaches and claims a method of increasing the activation or proliferation of T cells comprising contacting T cells with a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell (see entire document).
Chang teaches that an embodiment of the invention includes using microbeads that comprise a binding molecule that is an antibody to CD3 paired with another binding molecule that is specific for T cells, including an antibody to CD28 (see entire document, especially claims 1-2 and columns 11-12).
Chang et al. teach several methods for immobilizing antibodies on solid phase surfaces that are beads, including direct immobilization via a covalent modification (see especially columns 7-8), consistent with the claimed methods.

In response to previous arguments by applicant,
given the teachings of Chang that the same product used by June et al. in vitro could also be used in vivo, the ordinary artisan would have had a reasonable expectation that the method of June et al. could also be practiced in vivo. In view of the teachings of June et al. of the beneficial effect on T cell numbers when T cells are contacted with beads on which anti-CD3 and anti-CD28 have been co-immobilized, the ordinary artisan would have been motivated to administer the beads in vivo; particularly since an in vivo method would obviate potential sources of secondary infection due to ex vivo expansion of the T cells and would reduce the risk of exposure of health care workers to HIV infected cells.

In addition to the teachings of June et al. and Chang et al.,
Levine et al. teach the applicability of beads coated with both anti-CD3 antibodies and anti-CD28 antibodies in the stimulation of T cells of interest (see entire document, including Long-term Cell Cultures on page 893, column 1).

June et al. in view of Chang et al. and Levine et al. differ from the claims not measuring the level of CCR5 expression in T cells contacted with anti-CD3 antibodies and anti-CD28 antibodies.

As pointed out previously, Kwon et al. teach that the ligation of T cells with anti-CD3 antibodies and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

As noted previously, Allaway et al. teach various methods to measure CCR5, including in assays measuring the effects of inhibiting fusion of HIV-1 to $CD4^+$ T cells and infection of the cells (see entire document, including Summary of the Invention).

Given the teachings of the beneficial effects of contacting T cells with anti-CD3 and anti-CD28 antibodies to increase HIV resistance and that this beneficial effect was a result of down-regulation of CCR5 as taught by the prior art, one of ordinary skill in the art at the time the invention was made would have been motivated to monitor the expression of CCR5 expression to monitor the effect of combining anti-CD3 and anti-CD28 antibodies on T cell populations on HIV expression. In addition, the prior art provides for the co-immobilization of anti-CD3 and anti-CD28 on the same bead as a means of stimulating T cells. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. No claim allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/
Primary Examiner
Technology Center 1600
Art Unit 1644
June 29, 2009

4. OLD OLD OLD OLD

Waiting for dave's response waiting for dave's response

Claims 96-97 and 99-107 are rejected under 35 U.S.C. § 103(a) as being unpatentable over June et al. (U.S. Patent No. 6,352,694) ('694) (of record) AND/OR June et al. (U.S. Patent No. 6,905,680) ('680) in view of Chang et al. (U.S. Patent No. 6,129,916) (of record) and newly added Kwon et al. (U.S. Patent No. 5,569,997) and Allaway et al. (US 2004/0086528 A1).

The teachings of June et al. (U.S. Patent No. 6,352,694) in view of and Chang et al. (U.S. Patent No. 6,129,916) are of record.

A more thorough review of applicant's arguments and the examiner's rebuttal of record with respect to these teachings can be found in the previous Office Actions.

June et al. in view of Chang et al. differ from the claims not measuring the level of CCR5 expression in T cells contacted with anti-CD3 and anti-CD28 antibodies.

Newly added June et al. '680 provides for providing stimulating T cells from HIV-infected patients as well as for HIV-infected patients both in vitro and in vivo with anti-CD3 and anti-CD28 antibodies on the same solid surface, including beads (see entire document, including Summary of the Invention and Detailed Description of the Invention and Claims; also see Uses of the Methods of the Invention on columns 30-35). This reference further teaches the advantages of such procedures in providing for replenishing the immune response to said patients while providing HIV resistance (see Uses of the Methods of the Invention on columns 30-35 and Examples).

Although June et al. '680 teach the advantages of anti-CD3 and anti-CD28 antibody stimulation in the context of HIV-infected cells and treatment of HIV-infected patients, June et al. '680 does not teach the measuring CCR5 in the context of such treatment.

As pointed out previously, Kwon et al. teach that the ligation of T cells with anti-CD3 and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

Again, Allaway et al. teach various methods to measure CCR5, including in assays measuring the effects of inhibiting fusion of HIV-1 to $CD4^+$ T cells and infection of the cells (see entire document, including Summary of the Invention).

Given the teachings of the beneficial effects of contacting T cells with anti-CD3 and anti-CD28 antibodies to increase HIV resistance and that this beneficial effect was a result of down-regulation of CCR5 as taught by the prior art, one of ordinary skill in the art at the time the invention was made would have been motivated to monitor the expression of CCR5 expression

to monitor the effect of combining anti-CD3 and anti-CD28 antibodies on T cell populations on HIV expression. In addition, the prior art provides for the co-immobilization of anti-CD3 and anti-CD28 on the same bead as a means of stimulating T cells. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. Applicant's arguments, filed 9/7/095, have been fully considered but have not been found convincing essentially for the reasons of record and those addressed herein.

Applicant's arguments concerning the Levine, Science 272: 1939-1942 (1996) have been rendered moot in that this Levine reference is no longer a part of the rejection.

Kwon et al. was added previously to provide for the ligation of T cells with anti-CD3 and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

While applicant asserts that the prior art including the June '694, Chang, Kwon, and Allaway prior art references do not teach the advantages of the bead versus other solid phase surfaces, applicant is invited to the teachings of June et al. '680, indicated above. Note that the claims of both June '694 and '680 do claim providing the anti-CD3 and anti-CD28 antibodies on the same solid surface, including a bead, to achieve the claimed methods.

In response to applicant's arguments against the references individually, one cannot show non - obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 208 USPQ 871 (CCPA 1981). In re Merck & Co., Inc., 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of the references to monitor the effectiveness of stimulating T cells with anti-CD3 and anti-CD28 antibodies to replenish the immune response of HIV-infected patients with the additional advantages of increasing HIV-resistance via the CCR5 pathway in part, as taught by the prior art above.

In this case the teachings of the prior art pertaining to the issues of immunodeficiencies in HIV-infected patients also indicated success in the relevant ability of stimulating T cells with anti-CD3 and anti-CD28 antibodies on the same solid surface, including beads, to restore immune responsiveness in said patients, including increasing the resistance of said treated T cells to HIV infection and persistence to combine the references to solve a well known problem in the art by one of ordinary skill in the art at the time the invention was made. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that

some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

Applicant's arguments have not been found persuasive.